

**REMARKS**

In the Office Action dated August 19, 2008, claims 1, 2, 4, 8-10, 12 and 14-18, in the above-identified U.S. patent application were rejected. Reconsideration of the rejection is respectfully requested in view of the above amendments and the following remarks. Claims 1, 2, 4, 9-10, 12 and 15-18 remain in this application and claims 3, 5-8, 11 and 13-14 have been canceled.

Claims 1, 2, 4, 8-10, 12 and 14-18 were rejected under 35 USC §103(a) as unpatentable over Bleumer in view of Pavone. The office action indicates that the declarations filed in response to the previous Office Action are drawn to the specific combination of G250 antibody and IFN- $\alpha$ , whereas the pending claims refer to a combination of an anti-tumor antibody directed against the MN-antigen and an interferon. Claim 1 has been amended to indicate that antitumor antibody is a chimeric or humanized G250 antibody or a fragment thereof and the cytokine is IFN- $\alpha$ . In addition, applicants point out that Bleumer does not disclose a combination therapy comprising administration of both IFN- $\alpha$  and G250 but refers to a monotherapy with G250 antibody in order to evaluate both the safety and the response of RCC patients to a treatment with G250. This is clear from the fact that the patients pretreated with IFN- $\alpha$  received a medication break of at least 4 weeks before the beginning of G250 administration, resulting in a complete clearance of IFN- $\alpha$  before G250 was administered for the first time. Thus, applicants contend that Bleumer only teaches monotherapy of RCC by administering G250 antibody. Pavone does not cure the deficiencies in Bleumer as Pavone discloses low doses of recombinant IL-2 and recombinant IFN- $\alpha$  to induce a repeated and significant extension of CD3-CD56+ cells, which cells exhibit one of the most important lymphocyte

subsets for the immune response to tumoral mass (see page 86, last paragraph).

Pavone does not suggest or disclose that the combination of low doses of recombinant IL-2 and recombinant IFN- $\alpha$  are suitable for treating RCC. Pavone does not provide any data regarding the development of the patients' tumor mass following treatment with low doses of recombinant IL-2 and recombinant IFN- $\alpha$ . Therefore, applicants contend that Pavone does not teach a combination of low doses of recombinant IL 2 and recombinant IFN- $\alpha$  suitable for the treatment of RCC. Even if Pavone did teach a combination of IL2 and IFN-  $\alpha$  for the treatment of RCC (which Pavone does not), combining Pavone and Bleumer would result in a composition comprising G250 antibody, recombinant IFN- $\alpha$  in a low dose form and recombinant IL-2 in a low dose form. Since Pavone does not provide any indication that the described immunological effect would also be achieved by single administration of recombinant IFN- $\alpha$  in a low dose form (i.e. without additionally administering recombinant IL-2 in a low dose form), a person skilled in the art cannot arrive at a method for treating RCC comprising co-administering G250 antibody and IFN- $\alpha$  as the only active ingredients, as required by the present invention. The present situation is different from *In re Kerkhoven* as discussed in the office action. In the present situation, the active ingredients of the two references are not simply added together to arrive at the present invention. In order to arrive at the present invention, one skilled in the art would need to combine the active ingredients in Bleumer and Pavone and then delete recombinant IL-2 from the combination. Since there is no suggestion in either of these references that the recombinant IL-2 is unnecessary, such a combination is based on inadmissible hindsight. In view of the above discussion, applicants contend that one skilled in the art

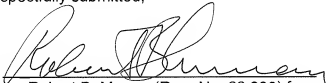
would not combine Bleumer and Pavone to arrive at the present invention and request that this rejection be withdrawn.

Applicants respectfully submit that all of claims 1, 2, 4, 9-10, 12 and 15-19 are now in condition for allowance. If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper. may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

By



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